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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,727	09/22/2003	George A. Scheele	JHU1710-6	9699

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 02/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,727	SCHEELE ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *32-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-31) in the reply filed on November 14, 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 32-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 14, 2005.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-26 and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-35 of U.S. Patent No. 6,835,717 ('717) in view of Khanna et al. The Journal of Clinical Investigation (2002), Vol. 109, pages 205-211 (Khanna) and Biggar et al. Lancet (1996), Vol. 347, page 1647 (Biggar).

The invention of the '717 patent differs from the instant claims in that the '717 patent is limited to the use of beta-cyclodextrins and does not read upon other cholesterol-sequestering agents; however, beta-cyclodextrin, and more specifically 2-OH-propyl-beta-cyclodextrin, is entirely within the scope of the instantly employed cholesterol-sequestering agents. The invention of the '717 patent also differs from the instant invention in that the method of the '717 patent is drawn to reducing the risk of sexually transmitting a pathogen/disease such as HIV, herpes virus, and hepatitis virus; however, it would have been obvious to one of ordinary skill in the art at the time of the invention to use cholesterol-sequestering agents to reduce the risk of maternal to fetal transmission of a pathogen/disease in view of the teachings of Khanna.

Khanna teaches that beta-cyclodextrins are water-soluble compounds that disrupt lipid rafts by adsorbing cholesterol from cellular membranes (page 206). Khanna further teaches that 2-OH-propyl-beta-cyclodextrin administered intravaginally prior to infected-cell challenge efficiently blocks virus transmission and induces minimal, if any damage to the vaginal mucosa.

Biggar presents a study which examined the efficacy of a birth canal washing procedure in reducing perinatal transmission of HIV-1 in Malawi. Biggar postulates that antiseptic cleansing of the birth canal might reduce the risk of perinatal infection. A clinical trial of the safety and efficacy of canal washing as a means to reduce HIV transmission. For the intervention group, treatment consisted of a manual cleansing of the vaginal introitus, the length and vault of the birth canal, the cervical os, and the presenting part of the infant with 0.25%chlorhexidine gluconate in sterile water, as well as washing of the infant. Cotton soaked in the solution and sufficiently damp to leave a residual solution in the vagina was wrapped around the examining fingers of a gloved hand. Chlorhexidine was chosen on the basis of an exceptionally good safety record (and some efficacy against group B streptotoccus), and because it can neutralize HIV.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ the instant method for preventing the transmission of a microorganism such as HIV in view of the teachings of Khanna. The '717 patent embraces methods where in cyclodextrin composition is administered intravaginally. Although the '717 patent is drawn to a method for reducing the risk of transmission of a sexually transmitted disease, one of ordinary skill in the art would readily recognize that pathogens such as HIV are transmitted by modes other than through sexual contact. One of ordinary skill in the art would also readily recognize that the virus does not discriminate between a sexual partner and fetus/infant in regards to vaginal transmission. Reduction of HIV transmission would provide sufficient motivation. Additional motivation is provided by Biggar which suggests washing the birth canal with

an agent known to neutralize HIV (chlorohexidine). Selection of an appropriate dosage regimen (i.e. dosage amount, concentration, time of administration, type of formulation, etc.) is well within the purview of the skilled artisan.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-31 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing maternal to fetal transmission of a microorganism using a beta-cyclodextrin composition, does not reasonably provide enablement for a method of preventing maternal to fetal transmission of a microorganism using beta-cyclodextrin or any other cholesterol-sequestering agent. The specification does not enable reducing maternal to fetal transmission of a microorganism using a cholesterol-sequestering agent other than beta-cyclodextrin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

1. the breadth of the claims;
2. the nature of the invention;
3. the state of the prior art;
4. the level of one of ordinary skill in the art;
5. the level of predictability in the art;
6. the amount of direction provided by the inventor;
7. the existence of working examples; and
8. the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Claims 1-31 are drawn to methods of reducing or preventing maternal to fetal transmission of a microorganism comprising administering to the birth canal of an individual a composition comprising a cholesterol-sequestering agent.

The USPTO applies to verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as the would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in applicant's specification. This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. Ordinary, simple English words whose meaning is clear and unquestionable, absent any indication that their use in a particular context changes their meaning, are construed to mean exactly what they say. While the claims of issued patents are interpreted in light of the specification, prosecution history, prior art and other claims, this is not the mode of

claim interpretation to be applied during examination. During examination, the claims must be interpreted as broadly as their terms reasonably allow. The ordinary and customary meaning of the term "prevent" is "to keep from happening : AVERT".

No examples are provided in the instant specification showing the prevention of maternal to fetal transmission of a microorganism by administering a composition comprising a cholesterol-sequestering agent. Hildreth US 6,835,717 (Hildreth) teaches that mechanical barriers such as condoms can be effective in preventing sexual transmission of HIV; however, topical microbicides currently available have proven inadequate, and the widely used surfactant microbicide, nonoxynol-9, which is used as a spermicide, may actually increase HIV infection by inducing genital ulcerations (columns 1-2). Due to the lack of guidance provided in the specification and the level of unpredictability in the art, one of ordinary skill in the art would not be able to practice the instant invention without undue experimentation.

Undue experimentation is also required to determine which compounds would be useful as cholesterol-sequestering agents and what sequestering agents would be effective to reduce maternal to fetal transmission of a microorganism. There has not been provided adequate guidance in the written description for accomplishing such, as only a limited number of compounds were assessed. While assays to determine if a compound acts as cholesterol-sequestering agents may have been available at the time of the invention, without guidance as to what molecules/compounds would likely posses this activity, undue trial and error experimentation would be required to screen through the myriad of different chemical molecules to determine those with the desired

cholesterol-sequestering activity and that would function in the claimed method of reducing or preventing maternal to fetal transmission of a microorganism.

It is noted that while there are some working examples using certain beta-cyclodextrins, it is not seen as sufficient to support the breath of the claims. The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to enable the use of any other compounds other than beta-cyclodextrins. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. See *In re Gardner* et al. 166 USPQ 138 (CCPA 1970).

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1 and 5-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims read upon pharmaceutical compositions comprising a "cholesterol-sequestering agent"; however, one of ordinary skill in the art would not be apprised of the metes and bounds of the instant invention as the sequestering agents are only described in functional terms. The term "cholesterol-sequestering agent" is not sufficient to convey a chemical structure, chemical name or the like to the instantly claimed "cholesterol-sequestering agent". There is nothing inherently wrong with defining some part of an invention in functional terms; however, a functional limitation

must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. Functional descriptions of chemical compounds/compositions must be coupled with a known or disclosed correlation between function and structure.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hildreth US 6,835,717 (Hildreth) in combination with Khanna et al. The Journal of Clinical Investigation (2002), Vol. 109, pages 205-211 (Khanna) and Biggar et al. Lancet (1996), Vol. 347, page 1647 (Biggar).

Claims 1-31 are drawn to methods of reducing or preventing maternal to fetal transmission of a microorganism comprising administering to the birth canal of an individual a composition comprising a cholesterol-sequestering agent.

Hildreth teaches methods of reducing the risk of transmission of a sexually transmitted pathogen by contacting the pathogen or cells susceptible to infection by the pathogen with a pharmaceutical composition comprising β-cyclodextrin (Abstract). The composition includes 1) a β-cyclodextrin and 2) a contraceptive, an agent for treating a sexually transmitted disease, a lubricant, or a combination thereof. The method is useful in reducing the risk of sexually transmitting pathogens, including enveloped virus such as HIV, HTLV, a herpes virus such as herpes simplex virus (HSV), bacterium, a yeast such as Candida, a mycoplasma, a protozoan, or a Chlamydia spp. (column 2). The cells susceptible to infection by the pathogen can be any cells depending, in part, on the pathogen, including epithelial cells, particularly vaginal epithelial or rectal epithelial cells. The HuPBL-SCID mouse model was used to examine the ability of the βCD derivative, 2-OH-βCD, to interrupt cell-associated transmission of HIV-1 (columns

13-16). Intravaginal administration of βCD prior to challenge by HIV-1 infected cells efficiently blocked virus transmission and induced minimal, if any, damage to the vaginal mucosa (Example 3). Since this agent is currently used for human administration, it will be recognized that 2-OH-βCD can be used alone, or in combination with other agents such as a contraceptive or antibiotic, to reduce the risk of transmission of sexually transmitted diseases. Antiviral agents that are useful include nucleoside analogs such as azacytidine. For topical administration, the βCD can be formulated in any pharmaceutically acceptable carrier, provided that the carrier does not affect the activity of the βCD in an undesirable manner. Thus, the composition can be, for example, in the form of a cream, a foam, a jelly, a lotion, an ointment, a solution, a spray, or a gel. Several mechanisms have been proposed by which HIV-1 is able to traverse the epithelium of the genitourinary tract to establish productive infection in lymph nodes. All of these mechanisms of transmission involve exposure of free virus to the extracellular environment, providing an opportunity, albeit a brief one, for virus specific intervention strategies to be effective at the mucosal surface.

Hildreth differs from the instantly claimed invention in that Hildreth does not explicitly state that the method is useful in reducing maternal to fetal transmission of a microorganism.

Khanna teaches that beta-cyclodextrins are water-soluble compounds that disrupt lipid rafts by adsorbing cholesterol from cellular membranes (page 206). Khanna further teaches that 2-OH-propyl-beta-cyclodextrin administered intravaginally

prior to infected-cell challenge efficiently blocks virus transmission and induces minimal, if any damage to the vaginal mucosa.

Biggar presents a study which examined the efficacy of a birth canal washing procedure in reducing perinatal transmission of HIV-1 in Malawi. Biggar postulates that antiseptic cleansing of the birth canal might reduce the risk of perinatal infection. A clinical trial of the safety and efficacy of canal washing as a means to reduce HIV transmission. For the intervention group, treatment consisted of a manual cleansing of the vaginal introitus, the length and vault of the birth canal, the cervical os, and the presenting part of the infant with 0.25%chlorhexidine gluconate in sterile water, as well as washing of the infant. Cotton soaked in the solution and sufficiently damp to leave a residual solution in the vagina was wrapped around the examining fingers of a gloved hand. Chlorhexidine was chosen on the basis of an exceptionally good safety record (and some efficacy against group B streptotoccus), and because it can neutralize HIV.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ the instant method for preventing the transmission of a microorganism such as HIV in view of the teachings of Khanna. Hildreth embraces methods where in cyclodextrin composition is administered intravaginally. Although the Hildreth is drawn to a method for reducing the risk of transmission of a sexually transmitted disease, one of ordinary skill in the art would readily recognize that pathogens such as HIV are transmitted by modes other than through sexual contact. One of ordinary skill in the art would also readily recognize that the virus does not discriminate between a sexual partner and fetus/infant in regards to vaginal

transmission. As taught by Hildreth all of the mechanisms of HIV vaginal transmission involve exposure of free virus to the extracellular environment, providing an opportunity, albeit a brief one, for virus specific intervention strategies to be effective at the mucosal surface. Reduction of HIV transmission would provide sufficient motivation. Additional motivation is provided by Biggar which suggests washing the birth canal with an agent known to neutralize HIV (chlorohexidine). Selection of an appropriate dosage regimen (i.e. dosage amount, concentration, time of administration, type of formulation, etc.) is well within the purview of the skilled artisan.

Conclusion

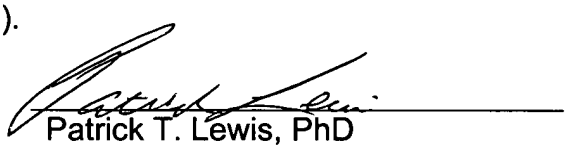
13. Claims 1-73 are pending. Claims 1-31 are rejected. Claims 32-73 are withdrawn from consideration as being drawn to a nonelected invention. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Patrick T. Lewis, PhD
Examiner
Art Unit 1623

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